Ref #	Hits	Search Query	DBs	Default Operator	Plurals	Time Stamp
L1	0	(Factor adj VIII) same (polyethylene adj glycol) and 558/6.ccls.	US-PGPUB; USPAT; EPO; DERWENT	OR	ON	2006/02/01 15:35
L2	1	(Factor adj VIII) same (polyethylene adj glycol) and 435/181.ccls.	US-PGPUB; USPAT; EPO; DERWENT	OR	ON	2006/02/01 15:36
L3	0	(Factor adj VIII) same (polyethylene adj glycol) and 260/112.5.ccls.	US-PGPUB; USPAT; EPO; DERWENT	OR	ON	2006/02/01 15:36
L4	0	(Factor adj VIII) same (polyethylene adj glycol) and 424/94.ccls.	US-PGPUB; USPAT; EPO; DERWENT	OR	ON	2006/02/01 15:36
L5	0	(Factor adj VIII) same (polyethylene adj glycol) and 424/117.ccls.	US-PGPUB; USPAT; EPO; DERWENT	OR	ON	2006/02/01 15:36
S1	0	(Factor adj VIII) and "polyethylene adj glycol"	US-PGPUB; USPAT; EPO; DERWENT	OR	ON	2004/12/13 13:48
S2	2388	(Factor adj VIII) and (polyethylene adj glycol)	US-PGPUB; USPAT; EPO; DERWENT	OR	ON	2004/12/13 13:50
S3	217112	S2 and B domain	US-PGPUB; USPAT; EPO; DERWENT	OR	ON	2004/12/13 13:50
S4	115	S2 and "B domain"	US-PGPUB; USPAT; EPO; DERWENT	OR	ON	2004/12/13 13:50
S5	117	(Factor adj VIII) same (polyethylene adj glycol)	US-PGPUB; USPAT; EPO; DERWENT	OR	ON	2006/02/01 15:35
S6	17	(Factor adj VIII) same (polyethylene adj glycol)and conjugate	US-PGPUB; USPAT; EPO; DERWENT	OR	ON	2004/12/13 13:58
S7	14	(Factor adj VIII) same (polyethylene adj glycol)and covalent	US-PGPUB; USPAT; EPO; DERWENT	OR	ON	2004/12/13 14:00

S8	1124	(Factor adj VIII) and (polyethylene adj glycol)and covalent	US-PGPUB; USPAT; EPO; DERWENT	OR	ON	2004/12/13 14:00
S9	6	(Factor adj VIII) adj30 (polyethylene adj glycol)and covalent	US-PGPUB; USPAT; EPO; DERWENT	OR	ON	2004/12/13 14:00
S10	6	(Factor adj VIII) adj50 (polyethylene adj glycol)and covalent	US-PGPUB; USPAT; EPO; DERWENT	OR	ON	2004/12/13 14:01
S11	6	(Factor adj VIII) adj100 (polyethylene adj glycol)and covalent	US-PGPUB; USPAT; EPO; DERWENT	OR	ON	2004/12/13 14:01
S12	7	(Factor adj VIII) near100 (polyethylene adj glycol)and covalent	US-PGPUB; USPAT; EPO; DERWENT	OR	ON	2004/12/13 14:38
S13	0	(Factor adj VIII) near (polyethylene adj glycol)and covalent	US-PGPUB; USPAT; EPO; DERWENT	OR	ON	2004/12/13 14:01
S14	42	(Factor adj VIII) and (polyethylene adj glycol)and covalent and polymer and "molecular weight" and "5000 Daltons"	US-PGPUB; USPAT; EPO; DERWENT	OR	ON	2004/12/13 15:35
S15	1	(Factor adj VIII) and (polyethylene adj glycol)and covalent and polymer and ("molecular weight" same "$000 Daltons")	US-PGPUB; USPAT; EPO; DERWENT	OR	ON	2004/12/13 15:36
S16	963	(Factor adj VIII) and (polyethylene adj glycol)and covalent and polymer	US-PGPUB; USPAT; EPO; DERWENT	OR	ON	2004/12/13 15:37
S17	281	(Factor adj VIII) and ((polyethylene adj glycol)same covalent) and polymer	US-PGPUB; USPAT; EPO; DERWENT	OR	ON	2004/12/13 15:37
S18	0	(Factor adj VIII) same ((polyethylene adj glycol)same covalent) and polymer	US-PGPUB; USPAT; EPO; DERWENT	OR	ON	2004/12/13 15:38
S19	0	(Factor adj VIII) same ((polyethylene adj glycol)same covalent) same polymer	US-PGPUB; USPAT; EPO; DERWENT	OR	ON	2004/12/13 15:38

S20	0	(Factor adj VIII) same ((polyethylene adj glycol)same covalent) same polymer and conjugate	US-PGPUB; USPAT; EPO; DERWENT	OR	ON	2004/12/13 15:38
S21	0	(Factor adj VIII) same ((polyethylene adj glycol)same covalent) and polymer and conjugate	US-PGPUB; USPAT; EPO; DERWENT	OR	ON	2004/12/13 15:38
S22	248	(Factor adj VIII) and ((polyethylene adj glycol)same covalent) and polymer and conjugate	US-PGPUB; USPAT; EPO; DERWENT	OR	ON	2004/12/13 15:39
S23	3	(Factor adj VIII) and ((polyethylene adj glycol)same covalent) and polymer and conjugate and "end capped"	US-PGPUB; USPAT; EPO; DERWENT	OR	ON	2004/12/13 15:40
S24	3	(Factor adj VIII) and ((polyethylene adj glycol)same covalent) and polymer and conjugate and "terminally capped"	US-PGPUB; USPAT; EPO; DERWENT	OR	ON	2004/12/13 15:41
S25	0	(Factor adj VIII) and ((polyethylene adj glycol)same covalent) and polymer and conjugate and ("6000" daltons)	US-PGPUB; USPAT; EPO; DERWENT	ADJ	ON	2004/12/13 15:42
S26	0	(Factor adj VIII) and ((polyethylene adj glycol)same covalent) and polymer and conjugate and ("6000 daltons")	US-PGPUB; USPAT; EPO; DERWENT	ADJ	ON	2004/12/13 15:42
S27	248	(Factor adj VIII) and ((polyethylene adj glycol)same covalent) and polymer and conjugate	US-PGPUB; USPAT; EPO; DERWENT	ADJ	ON	2004/12/13 15:42
S28	14	(Factor adj VIII) and ((polyethylene adj glycol)same covalent) and polymer and conjugate and "10000 daltons"	US-PGPUB; USPAT; EPO; DERWENT	ADJ	ON	2004/12/13 15:47
S29	24	(Factor adj VIII) and ((polyethylene adj glycol)and covalent) and polymer and conjugate and "10000 daltons"	US-PGPUB; USPAT; EPO; DERWENT	ADJ	ON	2004/12/13 15:48
S30	117	(Factor adj VIII) same "polyethylene glycol"	US-PGPUB; USPAT; EPO; DERWENT	ADJ	ON	2004/12/13 15:48
S31	17	(Factor adj VIII) same "polyethylene glycol" and conjugate	US-PGPUB; USPAT; EPO; DERWENT	ADJ	ON	2004/12/13 15:50

S32	0	(Factor adj VIII) same "polyethylene glycol" and conalent	US-PGPUB; USPAT; EPO; DERWENT	ADJ	ON	2004/12/13 15:50
S33	14	(Factor adj VIII) same "polyethylene glycol" and covalent	US-PGPUB; USPAT; EPO; DERWENT	ADJ	ON	2004/12/13 15:51
S34	0	(Factor adj VIII) same "polyethylene glycol" and covalent	EPO; DERWENT	ADJ	ON	2004/12/13 15:52
S35	2	(Factor adj VIII) same "polyethylene glycol" and "10000 daltons"	US-PGPUB; USPAT; EPO; DERWENT	ADJ	ON	2004/12/13 15:53
S36	4	(Factor adj VIII) same "polyethylene glycol" and "5000 daltons"	US-PGPUB; USPAT; EPO; DERWENT	ADJ	ON	2004/12/13 15:53
S37	0	"Factor vIII" same "polyethylene oxide" and lypholized	US-PGPUB; USPAT; EPO; DERWENT	OR	ON	2004/12/16 13:20
S38	0	"Factor vIII" and "polyethylene oxide" and lypholized	US-PGPUB; USPAT; EPO; DERWENT	OR	ON	2004/12/16 13:20
S39	100	"Factor vIII" and "polyethylene oxide" and lyophilized	US-PGPUB; USPAT; EPO; DERWENT	OR	ON	2004/12/16 13:20
S40	0	"Factor vIII" same "polyethylene oxide" and lyophilized	US-PGPUB; USPAT; EPO; DERWENT	OR	ON	2004/12/16 13:20
S41	100	"Factor vIII" and "polyethylene oxide" and lyophilized	US-PGPUB; USPAT; EPO; DERWENT	OR	ON	2004/12/16 13:20
S42	49	"Factor vIII" and "polyethylene oxide" and lyophilized and excipient	US-PGPUB; USPAT; EPO; DERWENT	OR	ON	2004/12/16 13:21
S43	1	"789956".ap. and conjugate	US-PGPUB; USPAT; EPO; DERWENT	OR	ON	2006/01/27 14:17
S44	0	"6037452".ap.	US-PGPUB; USPAT; EPO; DERWENT	OR	ON	2006/01/27 13:49

S45	2	"6037452".pn.	US-PGPUB; USPAT; EPO; DERWENT	OR	ON	2006/01/27 14:03
S46	6	"789956".ap.	US-PGPUB; USPAT; EPO; DERWENT	OR	ON	2006/01/27 14:17
S47	6	"789956".ap.	US-PGPUB; USPAT; EPO; DERWENT	OR	ON	2006/01/30 16:24
S48	2	"6037452".pn.	US-PGPUB; USPAT; EPO; DERWENT	OR	ON	2006/01/31 10:23
S49	0	"6037452".pn. and end with capped	US-PGPUB; USPAT; EPO; DERWENT	OR	ON	2006/01/30 16:48
S50	0	"6037452".pn. and capped	US-PGPUB; USPAT; EPO; DERWENT	OR	ON	2006/01/30 16:48
S51	0	"6037452".pn. and linear	US-PGPUB; USPAT; EPO; DERWENT	OR	ON	2006/01/30 16:48
S52	0	"6037452".pn. and branched	US-PGPUB; USPAT; EPO; DERWENT	OR	ON	2006/01/30 16:49
S53	0	"6037452".pn. and albumin	US-PGPUB; USPAT; EPO; DERWENT	OR	ON	2006/01/30 16:49
S54	0	"4179337".pn. and capped	US-PGPUB; USPAT; EPO; DERWENT	OR	ON	2006/01/30 16:56
S55	0	"4179337".pn. and amid	US-PGPUB; USPAT; EPO; DERWENT	OR	ON	2006/01/30 16:56
S56	1	"4179337".pn. and amide	US-PGPUB; USPAT; EPO; DERWENT	OR	ON	2006/01/30 17:09

S57	0	"4179337".pn. and thioether	US-PGPUB; USPAT; EPO; DERWENT	OR	ON	2006/01/30 17:09
S58	0	"4179337".pn. and disulfide	US-PGPUB; USPAT; EPO; DERWENT	OR	ON	2006/01/30 17:09
S59	0	"4179337".pn. and carbamate	US-PGPUB; USPAT; EPO; DERWENT	OR	ON	2006/01/30 17:11
S60	0	"5298643".pn. and carbamate	US-PGPUB; USPAT; EPO; DERWENT	OR	ON	2006/01/30 17:11
S61	0	"5298643".pn. and thioseter	US-PGPUB; USPAT; EPO; DERWENT	OR	ON	2006/01/30 17:11
S62	0	"5298643".pn. and thioester	US-PGPUB; USPAT; EPO; DERWENT	OR	ON	2006/01/31 09:24
S63	2898	polyethylene with glycol and end with capped	US-PGPUB; USPAT; EPO; DERWENT	OR	ON	2006/01/31 09:25
S64	596	polyethylene with glycol same end with capped	US-PGPUB; USPAT; EPO; DERWENT	OR	ON	2006/01/31 09:25
S65	39	polyethylene with glycol adj end with capped	US-PGPUB; USPAT; EPO; DERWENT	OR	ON	2006/01/31 09:58
S66	1	polyethylene with glycol adj end with capped and factor with vIII	US-PGPUB; USPAT; EPO; DERWENT	OR	ON	2006/01/31 09:26
S67	22	polyethylene with glycol adj end with capped and hydroxy	US-PGPUB; USPAT; EPO; DERWENT	OR	ON	2006/01/31 09:59
S68	23	polyethylene with glycol adj end with capped and methoxy	US-PGPUB; USPAT; EPO; DERWENT	OR	ON	2006/01/31 10:00

S69	9	polyethylene with glycol adj end with capped and albumin	US-PGPUB; USPAT; EPO; DERWENT	OR	ON	2006/01/31 10:02
S70	26	polyethylene with glycol adj end with capped and amide	US-PGPUB; USPAT; EPO; DERWENT	OR	ON	2006/01/31 10:03
S71	32	polyethylene with glycol adj end with capped and amine	US-PGPUB; USPAT; EPO; DERWENT	OR	ON	2006/01/31 10:03
S72	14	polyethylene with glycol adj end with capped and carbamate	US-PGPUB; USPAT; EPO; DERWENT	OR	ON	2006/01/31 10:05
S73	4	polyethylene with glycol adj end with capped and thioether	US-PGPUB; USPAT; EPO; DERWENT	OR	ON	2006/01/31 10:05
S74	8	polyethylene with glycol adj end with capped and disulfide	US-PGPUB; USPAT; EPO; DERWENT	OR	ON	2006/01/31 10:06
S75	0	"6037452".pn. and liquid	US-PGPUB; USPAT; EPO; DERWENT	OR	ON	2006/01/31 10:23
S76	2	"6037452".pn.	US-PGPUB; USPAT; EPO; DERWENT	OR	ON	2006/01/31 10:32
S77	2	"4,994,439".pn.	US-PGPUB; USPAT; EPO; DERWENT	OR	ON	2006/01/31 10:30
S78	1	"4179337".pn. and liquid	US-PGPUB; USPAT; EPO; DERWENT	OR	ON	2006/01/31 10:33
S79	0	"4179337".pn. and pharmaceutical with excipient	US-PGPUB; USPAT; EPO; DERWENT	OR	ON	2006/01/31 10:33
S80	0	"4179337".pn. and pharmaceutical with excepient	US-PGPUB; USPAT; EPO; DERWENT	OR	ON	2006/01/31 10:34

S81	0	"4179337".pn. and pharmaceutical with excipient	US-PGPUB; USPAT; EPO; DERWENT	OR	ON	2006/01/31 10:34
S82	0	"5,298,643".pn. and excipient	US-PGPUB; USPAT; EPO; DERWENT	OR	ON	2006/01/31 10:35
S83	0	"5,298,643".pn. and liquid	US-PGPUB; USPAT; EPO; DERWENT	OR	ON	2006/01/31 10:35
S84	2	"5,298,643".pn.	US-PGPUB; USPAT; EPO; DERWENT	OR	ON	2006/01/31 11:29
S85	0	"10154057".ap. and end with capped	US-PGPUB; USPAT; EPO; DERWENT	OR	ON	2006/01/31 11:29
S86	2	"154057".ap. and end with capped	US-PGPUB; USPAT; EPO; DERWENT	OR	ON	2006/01/31 11:32
S87	6	"154057".ap.	US-PGPUB; USPAT; EPO; DERWENT	OR	ON	2006/01/31 11:41
S88	328052	"154057".ap. branched	US-PGPUB; USPAT; EPO; DERWENT	OR	ON	2006/01/31 11:41
S89	3	"154057".ap. and branched	US-PGPUB; USPAT; EPO; DERWENT	OR	ON	2006/01/31 11:46
S90	3	"154057".ap. and branched and linear	US-PGPUB; USPAT; EPO; DERWENT	OR	ON	2006/01/31 12:49
S91	2	"154057".ap. and branched and amide	US-PGPUB; USPAT; EPO; DERWENT	OR	ON	2006/01/31 12:50
S92	2	"154057".ap. and amide and amine	US-PGPUB; USPAT; EPO; DERWENT	OR	ON	2006/01/31 12:50

S93	2	"154057".ap. and amide and amine and carbamate	US-PGPUB; USPAT; EPO; DERWENT	OR	ON	2006/01/31 12:51
S94	0	"154057".ap. and amide and amine and carbamate and thioether	US-PGPUB; USPAT; EPO; DERWENT	OR	ON	2006/01/31 12:51
S95	2	"154057".ap. and amide and amine and carbamate and disulfide	US-PGPUB; USPAT; EPO; DERWENT	OR	ON	2006/01/31 16:37
S96	0	"154057".ap. and excipinet	US-PGPUB; USPAT; EPO; DERWENT	OR	ON	2006/01/31 13:06
S97	2	"154057".ap. and excipient	US-PGPUB; USPAT; EPO; DERWENT	OR	ON	2006/01/31 13:06
S98	2	"154057".ap. and excipient and liquid	US-PGPUB; USPAT; EPO; DERWENT	OR	ON	2006/01/31 13:06
S99	0	"154057".ap. and disulfide and thioether	US-PGPUB; USPAT; EPO; DERWENT	OR	ON	2006/01/31 16:38
S100	2	"154057".ap. and disulfide	US-PGPUB; USPAT; EPO; DERWENT	OR	ON	2006/01/31 16:38
S101	6	"789956".ap.	US-PGPUB; USPAT; EPO; DERWENT	OR	ON	2006/02/01 14:42

```
  * * * * * * * * * * * * * * * STN  Columbus  * * * * * * * * * * * * * * * *

FILE 'HOME' ENTERED AT 15:43:16 ON 01 FEB 2006

=> index bioscience
FILE 'DRUGMONOG' ACCESS NOT AUTHORIZED
COST IN U.S. DOLLARS                                    SINCE FILE      TOTAL
                                                           ENTRY    SESSION
FULL ESTIMATED COST                                         0.21       0.21

INDEX 'ADISCTI, ADISINSIGHT, ADISNEWS, AGRICOLA, ANABSTR, ANTE, AQUALINE,
       AQUASCI, BIOENG, BIOSIS, BIOTECHABS, BIOTECHDS, BIOTECHNO, CABA, CAPLUS,
       CEABA-VTB, CIN, CONFSCI, CROPB, CROPU, DDFB, DDFU, DGENE, DISSABS, DRUGB,
       DRUGMONOG2, DRUGU, EMBAL, EMBASE, ...' ENTERED AT 15:43:30 ON 01 FEB 2006

70 FILES IN THE FILE LIST IN STNINDEX

Enter SET DETAIL ON to see search term postings or to view
search error messages that display as 0* with SET DETAIL OFF.

=> (Factor with VIII) (p) (polyethylene with glycol)
          0*  FILE ADISNEWS
          0*  FILE ANTE
          0*  FILE AQUALINE
          0*  FILE BIOENG
         22   FILE BIOSIS
         16*  FILE BIOTECHABS
         16*  FILE BIOTECHDS
          0*  FILE BIOTECHNO
  13 FILES SEARCHED...
         54   FILE CAPLUS
          0*  FILE CEABA-VTB
          0*  FILE CIN
          1   FILE DDFU
          1   FILE DISSABS
          2   FILE DRUGU
  29 FILES SEARCHED...
          0*  FILE ESBIOBASE
          0*  FILE FEDRIP
          0*  FILE FOMAD
  32 FILES SEARCHED...
          0*  FILE FOREGE
          0*  FILE FROSTI
          0*  FILE FSTA
         69   FILE IFIPAT
          2   FILE IMSDRUGNEWS
          1   FILE JICST-EPLUS
          0*  FILE KOSMET
          3   FILE LIFESCI
         15   FILE MEDLINE
          0*  FILE NTIS
          0*  FILE NUTRACEUT
          0*  FILE PASCAL
  50 FILES SEARCHED...
          0*  FILE PHARMAML
          2   FILE PROMT
         29   FILE TOXCENTER
        107   FILE USPATFULL
          3   FILE USPAT2
          0*  FILE WATER
         51   FILE WPIDS
  68 FILES SEARCHED...
         51   FILE WPINDEX
```

```
  18 FILES HAVE ONE OR MORE ANSWERS,   70 FILES SEARCHED IN STNINDEX

L1   QUE (FACTOR WITH VIII) (P) (POLYETHYLENE WITH GLYCOL)

=> d rank
F1          107   USPATFULL
F2           69   IFIPAT
F3           54   CAPLUS
F4           51   WPIDS
F5           51   WPINDEX
F6           29   TOXCENTER
F7           22   BIOSIS
F8           16*  BIOTECHABS
F9           16*  BIOTECHDS
F10          15   MEDLINE
F11           3   LIFESCI
F12           3   USPAT2
F13           2   DRUGU
F14           2   IMSDRUGNEWS
F15           2   PROMT
F16           1   DDFU
F17           1   DISSABS
F18           1   JICST-EPLUS


=> file caplus wpids toxcenter biosis medline
COST IN U.S. DOLLARS                            SINCE FILE      TOTAL
                                                     ENTRY    SESSION
FULL ESTIMATED COST                                   3.05       3.26

FILE 'CAPLUS' ENTERED AT 15:46:40 ON 01 FEB 2006
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
COPYRIGHT (C) 2006 AMERICAN CHEMICAL SOCIETY (ACS)

FILE 'WPIDS' ENTERED AT 15:46:40 ON 01 FEB 2006
COPYRIGHT (C) 2006 THE THOMSON CORPORATION

FILE 'TOXCENTER' ENTERED AT 15:46:40 ON 01 FEB 2006
COPYRIGHT (C) 2006 ACS

FILE 'BIOSIS' ENTERED AT 15:46:40 ON 01 FEB 2006
Copyright (c) 2006 The Thomson Corporation

FILE 'MEDLINE' ENTERED AT 15:46:40 ON 01 FEB 2006

=> (Factor with VIII) (p) (polyethylene with glycol)
L2          171 (FACTOR WITH VIII) (P) (POLYETHYLENE WITH GLYCOL)

=> dup remove
ENTER L# LIST OR (END):l2
PROCESSING COMPLETED FOR L2
L3          126 DUP REMOVE L2 (45 DUPLICATES REMOVED)

=> l3 and conjugate
L4           18 L3 AND CONJUGATE

=> d ti 1-18

L4   ANSWER 1 OF 18  CAPLUS  COPYRIGHT 2006 ACS on STN
TI   Peptides for blocking factor VIII inhibitors
```

L4 ANSWER 2 OF 18 CAPLUS COPYRIGHT 2006 ACS on STN
TI Polymer derivatives having particular atom arrangements in a linking group, their preparation, and use in compositions and as **conjugates**

L4 ANSWER 3 OF 18 CAPLUS COPYRIGHT 2006 ACS on STN
TI B-Domain Deleted Recombinant Coagulation **Factor VIII** Modified with Monomethoxy **Polyethylene Glycol**

L4 ANSWER 4 OF 18 CAPLUS COPYRIGHT 2006 ACS on STN
TI Poly(alkylene oxide)-blood coagulation factor VIII or factor IX **conjugates**

L4 ANSWER 5 OF 18 CAPLUS COPYRIGHT 2006 ACS on STN
TI Pharmaceutical composition comprising factor VIII and neutral liposomes

L4 ANSWER 6 OF 18 CAPLUS COPYRIGHT 2006 ACS on STN
TI Blood-coagulation factor VIII **conjugates**

L4 ANSWER 7 OF 18 WPIDS COPYRIGHT 2006 THE THOMSON CORP on STN
TI New protein **conjugate** comprising a physiologically active polypeptide, a non-peptide polymer and an immunoglobulin Fc fragment, useful for developing long-acting formulations of various drugs.

L4 ANSWER 8 OF 18 WPIDS COPYRIGHT 2006 THE THOMSON CORP on STN
TI Formulation, useful for pulmonary delivery of a therapeutic, prophylactic or diagnostic agent, which is useful to treat e.g. lung diseases, comprises a low molecular weight heparin and a therapeutic, prophylactic or diagnostic agent.

L4 ANSWER 9 OF 18 WPIDS COPYRIGHT 2006 THE THOMSON CORP on STN
TI **Conjugate** of biocompatible polymer-biologically active material, useful in therapeutic applications, comprises activated biocompatible polymer conjugated to carboxyl group of biologically active material.

L4 ANSWER 10 OF 18 WPIDS COPYRIGHT 2006 THE THOMSON CORP on STN
TI New active branched biocompatible polymers comprise long length of polymer linker with functional group to **conjugate** with biologically active proteins or peptides.

L4 ANSWER 11 OF 18 WPIDS COPYRIGHT 2006 THE THOMSON CORP on STN
TI Method for inducing tolerance to antigen - comprises administering antigen-polyethylene glycol **conjugate**, which suppresses humoral and cell-mediated immune responses.

L4 ANSWER 12 OF 18 WPIDS COPYRIGHT 2006 THE THOMSON CORP on STN
TI Cyclic imide thione activated poly alkylene oxide(s) - are used in preparation of **conjugates** with bioactive cpds. including peptide(s), proteins, antibodies, allergens, oligo nucleotide(s), etc..

L4 ANSWER 13 OF 18 TOXCENTER COPYRIGHT 2006 ACS on STN
TI Polymeric prodrug hydrogel depo formulations for peptides, proteins, and nucleotides

L4 ANSWER 14 OF 18 TOXCENTER COPYRIGHT 2006 ACS on STN
TI A pharmaceutical composition comprising a recombinant nonglycosylated immunoglobulin Fc region conjugated to a therapeutic protein as a drug carrier

L4 ANSWER 15 OF 18 TOXCENTER COPYRIGHT 2006 ACS on STN
TI Use of galactose oxidase for selective chemical conjugation of protractor molecules to glycoproteins of therapeutic or diagnostic interest

L4 ANSWER 16 OF 18 TOXCENTER COPYRIGHT 2006 ACS on STN
TI Cell-free in vitro glycoconjugation of interleukin 2 as therapeutic agent against cancer and AIDS in mammal and human

L4 ANSWER 17 OF 18 TOXCENTER COPYRIGHT 2006 ACS on STN
TI Glycan remodeling and glycoconjugation of peptides and proteins

L4 ANSWER 18 OF 18 TOXCENTER COPYRIGHT 2006 ACS on STN
TI Colloidal suspension of submicron particles for carrying active principles

=> d ab bib 1-12

L4 ANSWER 1 OF 18 CAPLUS COPYRIGHT 2006 ACS on STN
AB The invention discloses the use of a peptide comprising 8-15 amino acids for blocking the effect of FVIII inhibitors, the amino acid sequence simultaneously containing the following amino acids: at least two Tyr; at least one amino acid that carries a pos. or neg. total charge under physiol. conditions; at least one amino acid comprising a hydrophobic aromatic radical; an amino acid selected from the group consisting of Pro, Arg, Tyr or Phe, on the N-terminal end; and Asp, Phe, Arg, Lys or His on the C-terminal end. The amino acid sequence does not contain any Cys and/or Val-Val.
AN 2006:30532 CAPLUS
TI Peptides for blocking factor VIII inhibitors
IN Jungbauer, Alois
PA Austria
SO PCT Int. Appl., 51 pp.
CODEN: PIXXD2
DT Patent
LA German
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2006003183	A1	20060112	WO 2005-EP53139	20050701

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

PRAI EP 2004-15586 A 20040702
RE.CNT 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 2 OF 18 CAPLUS COPYRIGHT 2006 ACS on STN
AB Polymeric reagents comprise a moiety of atoms arranged in a specific order, where the moiety is positioned between a water-soluble polymer and a reactive group. The polymeric reagents are useful for, among other things, forming polymer-active agent **conjugates**.
AN 2005:14261 CAPLUS
DN 142:114733
TI Polymer derivatives having particular atom arrangements in a linking group, their preparation, and use in compositions and as **conjugates**
IN Harris, J. Milton; Kozlowski, Antoni; McManus, Samuel P.; Bentley, Michael D.; Charles, Stephen A.

PA Nektar Therapeutics AL, Corporation, USA
SO PCT Int. Appl., 113 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2005000360	A2	20050106	WO 2004-US16212	20040521
	WO 2005000360	A3	20050728		
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
	RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	CA 2510040	AA	20050106	CA 2004-2510040	20040521
	US 2005009988	A1	20050113	US 2004-851691	20040521
PRAI	US 2003-473213P	P	20030523		
	WO 2004-US16212	W	20040521		

L4 ANSWER 3 OF 18 CAPLUS COPYRIGHT 2006 ACS on STN
AB Recombinant coagulation factor VIII (r-VIII SQ) was chemical modified with monomethoxy poly(ethylene glycol) (mPEG). Three mPEG derivs. were used for coupling to the r-VIII SQ lysines, a mixed anhydride of monomethoxy poly(ethylene glycol) succinic acid (mPEG-SAH), monomethoxy poly(ethylene glycol) succinimidyl succinate (mPEG-SS), and monomethoxy poly(ethylene glycol) tresylate (mPEG-TRES). A consequence of the modification with all derivs. was a substantial reduction in coagulant activity, even at very low degrees of modification. A method was developed with the purpose of avoiding conjugation at certain important biol. sites on the factor VIII and thereby producing **conjugates** with better retained activity. This was achieved by immobilizing the protein onto a solid matrix during the modification reaction. Characterization of **conjugates** by SDS-PAGE, western blots, interaction with von Willebrand factor (vWf), and thrombin activation/inactivation analyses was undertaken. The SDS-PAGE and western blots revealed coupling heterogeneity regarding degree of modification. The amount of factor VIII able to bind to vWf decreased with the conjugation. Thrombin activated the modified factor VIII to essentially the same extent as the reference preparation of r-VIII SQ. Inactivation of the modified factor VIII was, however, slower than inactivation of the unmodified protein. Finally, an in vitro study was performed to evaluate the influence of the mPEG modification on the protein stability in extract of porcine tissue. Despite that **conjugates** with low degrees of modification were included in the study, the coagulant activity was preserved to a significantly higher extent in all incubation mixts. containing **conjugates** compared to that with unmodified protein.
AN 2000:214917 CAPLUS
DN 133:125062
TI B-Domain Deleted Recombinant Coagulation **Factor VIII** Modified with Monomethoxy **Polyethylene Glycol**
AU Roestin, Johanna; Smeds, Anna-Lisa; Aakerblom, Eva
CS Recombinant Factor VIII R&D, Pharmacia & Upjohn, Stockholm, S-112 87, Swed.
SO Bioconjugate Chemistry (2000), 11(3), 387-396
CODEN: BCCHES; ISSN: 1043-1802
PB American Chemical Society

DT Journal
LA English
RE.CNT 36 THERE ARE 36 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 4 OF 18 CAPLUS COPYRIGHT 2006 ACS on STN
AB Blood-coagulation factor VIIIC:von Willebrand factor, factor VIII:C, or factor IX or the activated factors are covalently linked to a poly(alkylene oxide). The resulting **conjugates** have improved stability and decreased immunogenicity.
AN 2000:169386 CAPLUS
DN 132:212666
TI Poly(alkylene oxide)-blood coagulation factor VIII or factor IX **conjugates**
IN Minamino, Hitoshi; Mealey, Edward H.
PA Alpha Therapeutic Corporation, USA
SO U.S., 6 pp.
CODEN: USXXAM
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI US 6037452	A	20000314	US 1992-866518	19920410
PRAI US 1992-866518		19920410		

RE.CNT 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 5 OF 18 CAPLUS COPYRIGHT 2006 ACS on STN
AB A pharmaceutical composition for parenteral administration comprising a therapeutically effective amount of a protein or polypeptide and substantially neutral colloidal particles. The particles comprise approx. 1-20 mol% of an amphipathic lipid derivatized with a biocompatible hydrophilic polymer which carries substantially no net charge. The protein or polypeptide is capable of externally binding the colloidal particles, or is capable of binding PEG, and is not encapsulated in the colloidal particles. A preferred protein is **factor VIII** , whose half-life is extended and which is protected from serum inhibitor antibodies by injecting it as a component of the composition Egg phosphatidylcholine (EPC) and distearoylphosphatidylethanolamine-Me **polyethylene glycol** 2000 (DSPE-PEG 2000) were weighed i.m. a ratio of 80:20 (5% molar ratio of DSPE-PEG 2000), resp., dissolved in 10% in tert-BuOH, and the solution was lyophilized. The dry lipid powder obtained was resuspended at 10% in a buffer containing 130 mM NaCl, 10 mM sodium citrate, pH 7.0 1 mM CaCl2 to form liposomes. The liposomes were filtered in an extruder apparatus through polycarbonate filters (1.2, 0.2 and 0.1 μm) to form liposomes (120-140 nm). The **factor VIII** was formulated into liposomes and the pharmacokinetic parameters were determined
AN 1999:708582 CAPLUS
DN 131:327532
TI Pharmaceutical composition comprising factor VIII and neutral liposomes
IN Baru, Moshe; Bar, Liliana; Nur, Israel
PA Opperbas Holding B.V., Neth.
SO PCT Int. Appl., 31 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 9955306	A1	19991104	WO 1999-IL217	19990423
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ,				

DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

CA	2329768	AA	19991104	CA 1999-2329768	19990423
AU	9934414	A1	19991116	AU 1999-34414	19990423
AU	747391	B2	20020516		
BR	9909978	A	20001226	BR 1999-9978	19990423
EP	1079805	A1	20010307	EP 1999-916022	19990423
EP	1079805	B1	20041124		

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI

JP	2002512947	T2	20020508	JP 2000-545506	19990423
AT	283034	E	20041215	AT 1999-916022	19990423
PT	1079805	T	20050331	PT 1999-916022	19990423
ES	2233036	T3	20050601	ES 1999-916022	19990423
US	6593294	B1	20030715	US 2000-673412	20001122
US	2003134778	A1	20030717	US 2002-327970	20021226
US	6930087	B2	20050816		
PRAI IL	1998-124224	A	19980427		
WO	1999-IL217	W	19990423		
US	2000-673412	A3	20001122		

RE.CNT 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 6 OF 18 CAPLUS COPYRIGHT 2006 ACS on STN

AB The blood-coagulation **factor VIII** is conjugated to nonantigenic ligands, such as polysaccharides, sialic acid, albumin, von Willebrand factor and **polyethylene glycol**. **Factor VIII** was coupled to NaIO4- oxidized dextran in 1M NaCl and 0.05 M NaAcO, at pH 6. When infused into the bloodstream of hemophilic dogs the conjugated **factor VIII** had longer half-life than the native **factor VIII**.

AN 1991:214411 CAPLUS
DN 114:214411
TI Blood-coagulation factor VIII **conjugates**
IN Fulton, Anne J.; Johnson, Alan J.
PA New York University, USA
SO U.S., 13 pp. Cont.-in-part of U.S. 4,847,362.
CODEN: USXXAM
DT Patent
LA English
FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 4970300	A	19901113	US 1989-298413	19890118
	US 4743680	A	19880510	US 1985-697267	19850201
	US 4847362	A	19890711	US 1987-122372	19871119
	US 4952675	A	19900828	US 1988-291516	19881229
PRAI	US 1985-697267	A1	19850201		
	US 1987-122372	A2	19871119		

L4 ANSWER 7 OF 18 WPIDS COPYRIGHT 2006 THE THOMSON CORP on STN

AB WO2005047336 A UPAB: 20050621
NOVELTY - Protein **conjugate** comprising covalently linked physiologically active polypeptide, a non-peptide polymer and immunoglobulin Fc fragment is new.
DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for:
(A) a method for preparing the protein **conjugate**; and

(B) a pharmaceutical composition for enhancing in vivo duration and stability of a physiologically active polypeptide comprising the protein **conjugate** and a pharmaceutical carrier.

USE - The protein **conjugate** is useful for developing long-acting formulations of various polypeptide drugs. The protein **conjugate** and composition are useful for enhancing in vivo duration and stability of a physiologically active polypeptide.

ADVANTAGE - The protein **conjugates** have enhanced serum stability without reducing the in vivo activity of the bound peptides.

Fab'-N-PEG-N-Fc complex was subjected to pharmacokinetic analysis using Fab' as a control by subcutaneous injection into rats at 100 micro g/kg and blood samples taken at 1, 6, 12, 24, 30, 48, 72, 96, 120, 240 and 288 hours examined by ELISA for serum protein levels. By 240 hours, serum protein concentration of unconjugated Fab' had fallen below 1 ng/ml compared with 100 ng/ml for the complex.

Dwg.0/15

AN 2005-386334 [39] WPIDS

CR 2005-367003 [37]; 2005-372351 [38]; 2005-372352 [38]

DNC C2005-119573

TI New protein **conjugate** comprising a physiologically active polypeptide, a non-peptide polymer and an immunoglobulin Fc fragment, useful for developing long-acting formulations of various drugs.

DC A96 B04 B05 D16

IN BAE, S M; KIM, D J; KIM, Y M; KWON, S C; LEE, G S; LIM, C K

PA (HANM-N) HANMI PHARM CO LTD

CYC 107

PI WO 2005047336 A1 20050526 (200539)* EN 126

RW: AT BE BG BW CH CY CZ DE DK EA EE ES FI FR GB GH GM GR HU IE IS IT KE LS LU MC MW MZ NA NL OA PL PT RO SD SE SI SK SL SZ TR TZ UG ZM ZW

W: AE AG AL AM AT AU AZ BA BB BG BR BW BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE EG ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NA NI NO NZ OM PG PH PL PT RO RU SC SD SE SG SK SL SY TJ TM TN TR TT TZ UA UG US UZ VC VN YU ZA ZM ZW

ADT WO 2005047336 A1 WO 2004-KR2944 20041113

PRAI KR 2003-80299 20031113

L4 ANSWER 8 OF 18 WPIDS COPYRIGHT 2006 THE THOMSON CORP on STN

AB WO2005032483 A UPAB: 20050512

NOVELTY - Formulation (A) for pulmonary delivery of a therapeutic, prophylactic, or diagnostic agent comprises a low molecular weight heparin (LMWH) and a therapeutic, prophylactic, or diagnostic agent (1).

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for:

(A) a heparin, modified such that the anti-Xa activity and/or anti-IIa activity of the heparin is reduced by at least 50% or more as compared to a reference standard;

(B) a method of making a LMWH for pulmonary delivery of a therapeutic, prophylactic, or diagnostic agent, comprising providing a LMWH, and modifying the LMWH such that anti-Xa activity and/or anti-IIa activity is reduced by at least 50% or more than a reference standard;

(C) a method of preparing a formulation for pulmonary delivery of an active agent comprising combining an active agent, and a LMWH; and

(D) a method of delivering (1) to a subject, comprising administering (A) to the pulmonary tissue of a subject.

ACTIVITY - Respiratory-Gen.; Antidiabetic; Endocrine-Gen.; Vulnerary; Antiemetic; Cytostatic; CNS-Gen.; Nephrotropic.

MECHANISM OF ACTION - alpha -1 Proteinase inhibitor; Cystic fibrosis transmembrane conductance regulator; Tissue plasminogen activator.

USE - Formulation (A) is useful for pulmonary delivery of a therapeutic, prophylactic, or diagnostic agent (claimed), which is useful to treat e.g. a respiratory disease or a lung disease, diabetes, Turner's syndrome, trauma, cystic fibrosis and chronic renal insufficiency.It is

also used in radiation therapy.

ADVANTAGE - The bioavailability of (1) is at least 10% greater than the bioavailability of (1) in the absence of the heparin (claimed). The bioavailability of (1) is preferably at least 90% greater than the bioavailability of (1) in the absence of the heparin. The pulmonary delivery of (A) to the lung produces a local effect for the treatment of respiratory diseases. The bioavailability of insulin (when delivered with LMWH) is 100000 micro-IU/ml in 1-2 hours after delivery.

The bioavailability of insulin formulated with LMWH was tested in rats. The results showed that plasma insulin level was 1200000 micro-IU/ml.

Dwg.0/6

AN 2005-296018 [30] WPIDS

DNC C2005-091509

TI Formulation, useful for pulmonary delivery of a therapeutic, prophylactic or diagnostic agent, which is useful to treat e.g. lung diseases, comprises a low molecular weight heparin and a therapeutic, prophylactic or diagnostic agent.

DC B05 B07

IN PICARD, M; QI, Y; RICHARDSON, T; VENKATARAMAN, G; QI, Y W

PA (PICA-I) PICARD M; (QIYY-I) QI Y; (RICH-I) RICHARDSON T; (VENK-I) VENKATARAMAN G; (MOME-N) MOMENTA PHARM INC

CYC 108

PI WO 2005032483 A2 20050414 (200530)* EN 89

RW: AT BE BG BW CH CY CZ DE DK EA EE ES FI FR GB GH GM GR HU IE IT KE LS LU MC MW MZ NA NL OA PL PT RO SD SE SI SK SL SZ TR TZ UG ZM ZW

W: AE AG AL AM AT AU AZ BA BB BG BR BW BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE EG ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NA NI NO NZ OM PG PH PL PT RO RU SC SD SE SG SK SL SY TJ TM TN TR TT TZ UA UG US UZ VC VN YU ZA ZM ZW

US 2005207988 A1 20050922 (200563)

ADT WO 2005032483 A2 WO 2004-US32613 20041001; US 2005207988 A1 Provisional US 2003-508062P 20031001, Provisional US 2004-580869P 20040618, US 2004-957218 20041001

PRAI US 2004-580869P 20040618; US 2003-508062P 20031001; US 2004-957218 20041001

L4 ANSWER 9 OF 18 WPIDS COPYRIGHT 2006 THE THOMSON CORP on STN

AB WO2004084948 A UPAB: 20041109

NOVELTY - A **conjugate** (I) of biocompatible polymer-biologically active material, comprises an activated biocompatible polymer conjugated to a carboxyl group or C-terminus of biologically active material at a molar ratio of 1:1.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

(1) pharmaceutical composition (PC) comprising (I) and a carrier;

(2) preparing (M1) a **conjugate** of biocompatible polymer-biologically active material, involves the step of conjugating the biologically active material to the activated biocompatible polymer with the stepwise addition of coupling reagent under the condition in which the molar ratio of biologically active material to activated biocompatible polymer is 1:1-1:20, the ratio of biologically active material to the coupling reagent is 1:1-1:50, and pH is in the range of 2-5; and

(3) **conjugate** of biocompatible polymer-biologically active material prepared by (M1), where the **conjugate** comprises an activated biocompatible polymer conjugated to a carboxyl group or C-terminus of biologically active material at a molar ratio of 1:1.

ACTIVITY - None given.

MECHANISM OF ACTION - Immunostimulator. No supporting data is given.

USE - (I) e.g. an antibody-PEG **conjugate**, or PC is useful in therapeutic applications, and disease treatment and prevention.

ADVANTAGE - (I) exhibits therapeutic efficacy up to 20-fold higher

than native (non-conjugated) proteins as they have an extended half-life and higher stability compared to native proteins. (I) has increased stability in vivo, bioavailability and half-life. (I) retains the biological activity of biologically active material by preventing the attachment of polymers to active sites. (I) reduces the injection intervals from daily or once per two days to weekly or biweekly injection, thus the toxicity and side effects of drugs by frequent administration are reduced substantially.

DESCRIPTION OF DRAWING(S) - The figure shows the graph representing the plasma half-life of mPEG(20000)-Hz-G-CSF, native G-CSF and Neulasta. Dwg.8/20

AN 2004-737257 [72] WPIDS

DNC C2004-259199

TI **Conjugate** of biocompatible polymer-biologically active material, useful in therapeutic applications, comprises activated biocompatible polymer conjugated to carboxyl group of biologically active material.

DC A96 B04

IN PARK, M; CHA, G H; KIM, J H; LEE, G W; PARK, M O; JACOBS, J W

PA (BIOP-N) BIOPOLYMED INC; (BIOP-N) BIOPOLYMED; (PARK-I) PARK M; (JACO-I) JACOBS J W

CYC 109

PI WO 2004084948 A1 20041007 (200472)* EN 66
RW: AT BE BG BW CH CY CZ DE DK EA EE ES FI FR GB GH GM GR HU IE IT KE LS LU MC MW MZ NL OA PL PT RO SD SE SI SK SL SZ TR TZ UG ZM ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BW BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE EG ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NA NI NO NZ OM PG PH PL PT RO RU SC SD SE SG SK SL SY TJ TM TN TR TT TZ UA UG US UZ VC VN YU ZA ZM ZW
KR 2004086521 A 20041011 (200512)
US 2005059129 A1 20050317 (200521)
EP 1608408 A1 20051228 (200603) EN
R: AL AT BE BG CH CY CZ DE DK EE ES FI FR GB GR HU IE IT LI LT LU LV MC MK NL PL PT RO SE SI SK TR
US 2005281778 A1 20051222 (200603)

ADT WO 2004084948 A1 WO 2004-KR701 20040327; KR 2004086521 A KR 2004-7983 20040206; US 2005059129 A1 CIP of WO 2004-KR701 20040327, US 2004-947513 20040922; EP 1608408 A1 EP 2004-723918 20040327, WO 2004-KR701 20040327; US 2005281778 A1 Cont of WO 2004-KR701 20040327, CIP of US 2004-947513 20040922, US 2005-187522 20050722

FDT EP 1608408 A1 Based on WO 2004084948

PRAI KR 2004-7983 20040206; KR 2003-19734 20030328;
KR 2003-7983 20040206

L4 ANSWER 10 OF 18 WPIDS COPYRIGHT 2006 THE THOMSON CORP on STN

AB WO 200209766 A UPAB: 20040218
NOVELTY - Active branched biocompatible polymer derivatives (I) comprising a long length of polymer linker with functional group to **conjugate** with biologically active proteins or peptides, are new.

DETAILED DESCRIPTION - An INDEPENDENT CLAIM is included for protein-polymer or peptide-polymer **conjugates** produced by reaction of (I) with biologically active protein or peptide.

ACTIVITY - None given in the source material.

MECHANISM OF ACTION - None given in the source material.

USE - Used for producing protein-polymer or peptide-polymer **conjugates** (claimed) useful as therapeutic drugs in medicines.

ADVANTAGE - The linker **conjugates** a reduced number of polymer derivatives to the active sites of proteins, and does not decrease the biological activity of the proteins or peptides. The **conjugates** are stable from protease degradation, have improved water solubility, reduce the steric hindrance in active sites of proteins and retain the biological activity for a long period of time, thus have improved bioavailability of the bioactive proteins and peptides. The

protein-polymer or peptide-polymer **conjugates** minimize the number of administrations and are capable of decreasing the side effects in accordance with over drug abuse.
Dwg.0/5
AN 2002-303913 [34] WPIDS
DNC C2002-088338
TI New active branched biocompatible polymers comprise long length of polymer linker with functional group to **conjugate** with biologically active proteins or peptides.
DC A96 B04 D16
IN CHO, S H; LEE, K C; PARK, M O; CHO, S
PA (LEEK-I) LEE K; (PARK-I) PARK M; (LEEK-I) LEE K C; (PARK-I) PARK M O
CYC 96
PI WO 2002009766 A1 20020207 (200234)* EN 47
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW
AU 2002024597 A 20020213 (200238)
KR 2002010363 A 20020204 (200254)
KR 396983 B 20030902 (200412)
ADT WO 2002009766 A1 WO 2001-KR1209 20010713; AU 2002024597 A AU 2002-24597 20010713; KR 2002010363 A KR 2000-44046 20000729; KR 396983 B KR 2000-44046 20000729
FDT AU 2002024597 A Based on WO 2002009766; KR 396983 B Previous Publ. KR 2002010363
PRAI KR 2000-44046 20000729

L4 ANSWER 11 OF 18 WPIDS COPYRIGHT 2006 THE THOMSON CORP on STN
AB WO 9851341 A UPAB: 19990127
Method for inducing tolerance to antigen (Ag), comprises administering antigen-**polyethylene glycol conjugate** (I), which suppresses humoral and cell-mediated immune responses against Ag. Also claimed are: (1) a method for obtaining passive transfer of suppression of an immune response comprising: (a) treating an animal with (I), and (b) transferring lymphocytes from the animal to a syngeneic recipient animal, where the lymphocytes provide suppression of Ag-specific CTL activity in the recipient animal, and (2) a method for conducting gene therapy comprising administering an immuno-suppressive tolerogenic **conjugate**, consisting of a protein (P) coupled to monomethoxypolyethylene glycol (mPEG) with a molecular weight 2000-10000 Da, one day prior to administration of the gene therapy vector encoding a gene for (P) which is identical to (P) conjugated to mPEG, so that tolerance to (P) is induced.
USE - The methods are used in the treatment of allergies, and autoimmune diseases. they are also used to prevent an immune rejection of organ transplants or transplants of DNA transfected cells, by administering (I) in the recipient prior to transplantation. (I) can also be used in the treatment of organ-specific autoimmune diseases, where (I) comprises an auto-Ag. The methods are especially useful in the treatment of haemophilia by administering human blood factor (especially human clotting blood **factor VIII** and human blood factor IV)-mPEG **conjugate**. In gene therapy tolerance towards the vector protein is also induced prior to administration of the gene therapy vector (all claimed).
Dwg.0/10
AN 1999-045195 [04] WPIDS
DNC C1999-014104
TI Method for inducing tolerance to antigen - comprises administering antigen-polyethylene glycol **conjugate**, which suppresses humoral and cell-mediated immune responses.

DC A96 B04 D16
IN KAPP, J A; KE, Y; LANG, G M; SEHON, A H
PA (UYEM-N) UNIV EMORY; (UYMA-N) UNIV MANITOBA
CYC 22
PI WO 9851341 A1 19981119 (199904)* EN 99
RW: AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE
W: AU CA JP US
AU 9874853 A 19981208 (199916)
ADT WO 9851341 A1 WO 1998-US9786 19980514; AU 9874853 A AU 1998-74853 19980514
FDT AU 9874853 A Based on WO 9851341
PRAI US 1997-46469P 19970514

L4 ANSWER 12 OF 18 WPIDS COPYRIGHT 2006 THE THOMSON CORP on STN
AB WO 9417039 A UPAB: 19940928
Water soluble cyclic imide thione (CIT) activated polyalkylene oxides (PAO) are new. Pref., CIT activated PAO are of formula X-R-L-CO-R3 (II); where R = a water soluble PAO; X = the PAO terminal gp.; R3 = a CIT, with the imido gp. covalently bonded to the CO gp.; and L = a gp. forming a hydrolytically stable, covalently bonded linkage between the PAO and CO gps.

The PAO is either a **polyethylene glycol** (PEG) or a block copolymer of PEG and polypropylene glycol, with M.weight 2-20, pref. 5 kD average, X is 1-4C alkoxy, especially methoxy, or is L-CO-R3, R3 is e.g. gps. (a); L = e.g. O, NH, OCH2, NHCO(CH2)z, NHCO(CH2)zO, CONH(CH2)z, S, CONH(CH2)zO, etc., in which z = 1-10.

USE/ADVANTAGE - CIT activated PAO are used to form biologically active **conjugates** with biologically active nucleophiles. It is known that conjugation with PAO reduces immunogenicity and antigenicity, and they persist longer in the bloodstream than the unmodified bioactive material. Examples of conjugation use are for insulin, tissue plasminogen activator, interleukins, haemoglobin, enzymes of various types, serum proteins (e.g., **Factors VIII** and IX), immunoglobulins, lectins, interferons, CSFs ovalbumin, BSA, ACTH, glucagon, somatostatin, somatotropin, thymosin, etc., hypothalamic releasing factors, prolactin, chorionic gonadotrophin, and allergen proteins, which, with reduced allergenicity, can be used as tolerance inducers. The CIT activated PAO have superior hydrolytic stability to prior art cpds. with reactive functional gps., e.g. PAO NHS carbonates typically have half life of 2 hrs. at pH 7; for the CIT cpds., a range 10-120 hrs., dependent on needs, is quoted. This permits bulk solns. to be made in advance of production, less hydrolytic degradation in reaction, increased yields and lower process costs.

Dwg.0/0
AN 1994-263988 [32] WPIDS
DNC C1994-120788
TI Cyclic imide thione activated poly alkylene oxide(s) - are used in preparation of **conjugates** with bioactive cpds. including peptide(s), proteins, antibodies, allergens, oligo nucleotide(s), etc..
DC A25 A96 B04
IN GREENWALD, R B; MARTINEZ, A J; MARTINEZ, A
PA (ENZO-N) ENZON INC
CYC 39
PI WO 9417039 A1 19940804 (199432)* EN 24
RW: AT BE CH DE DK ES FR GB GR IE IT LU MC NL PT SE
W: AU BG BR CA CZ FI HU JP KP KR LK MG MN MW NO NZ PL PT RO RU SE SK UA
US 5349001 A 19940920 (199437) 7
AU 9460892 A 19940815 (199444)
US 5405877 A 19950411 (199520) 7
EP 681572 A1 19951115 (199550) EN
R: CH DE DK FR GB IE LI NL
JP 08506131 W 19960702 (199650) 23
EP 681572 B1 20010905 (200152) EN

R: CH DE DK FR GB IE LI NL
DE 69428189 E 20011011 (200168)
JP 3294849 B2 20020624 (200243) 8
CA 2154170 C 20041214 (200501) EN
ADT WO 9417039 A1 WO 1994-US578 19940118; US 5349001 A US 1993-6247 19930119; AU 9460892 A AU 1994-60892 19940118; US 5405877 A Div ex US 1993-6247 19930119, US 1994-297651 19940829; EP 681572 A1 EP 1994-907229 19940118, WO 1994-US578 19940118; JP 08506131 W JP 1994-517145 19940118, WO 1994-US578 19940118; EP 681572 B1 EP 1994-907229 19940118, WO 1994-US578 19940118; DE 69428189 E DE 1994-628189 19940118, EP 1994-907229 19940118, WO 1994-US578 19940118; JP 3294849 B2 JP 1994-517145 19940118, WO 1994-US578 19940118; CA 2154170 C CA 1994-2154170 19940118, WO 1994-US578 19940118
FDT AU 9460892 A Based on WO 9417039; US 5405877 A Div ex US 5349001; EP 681572 A1 Based on WO 9417039; JP 08506131 W Based on WO 9417039; EP 681572 B1 Based on WO 9417039; DE 69428189 E Based on EP 681572, Based on WO 9417039; JP 3294849 B2 Previous Publ. JP 08506131, Based on WO 9417039; CA 2154170 C Based on WO 9417039
PRAI US 1993-6247 19930119